

Amendments to the Claims

1-28. (Cancelled)

29. (Currently Amended) A method for producing a genetically modified lymphoid cell capable of directed and selective genetic diversification of a transgenic target nucleic acid sequence by hypermutation comprising transfecting a lymphoid cell with a genetic construct comprising said target nucleic acid sequence into the immunoglobulin locus of said lymphoid cell to produce said genetically modified lymphoid cell, wherein said lymphoid cell contains no deleterious mutations in genes encoding XRCC2, XRCC3, or RAD51 proteins or their analogues, said lymphoid cell is capable of gene conversion prior to transfection, and said hypermutation in said genetically modified lymphoid cell occurs at a rate higher than the background mutation rate of mutation in said lymphoid cell.

30. (Withdrawn) The method according to claim 29, wherein said genetic construct further comprises a nucleic acid sequence capable of serving as a gene conversion donor for said target nucleic acid sequence.

31-34. (Cancelled)

35. (Previously Presented) The method according to claim 29, wherein transfecting said lymphoid cell comprises inserting said target nucleic acid sequence into said immunoglobulin locus of said lymphoid cell by targeted integration.

36-43. (Cancelled)

44. (Previously Presented) The method according to claim 29, wherein an endogenous V-gene or a fragment thereof in said lymphoid cell is replaced with said target nucleic acid sequence.

45. (Previously Presented) The method according to claim 29, wherein said lymphoid cell is capable of homologous recombination and DNA repair.

46. (Previously Presented) The method according to claim 29, wherein said lymphoid cell is an immunoglobulin-expressing B cell.

47. (Previously Presented) The method according to claim 29, wherein said lymphoid cell is derived from chicken, sheep, cow, pig, or rabbit.

48. (Previously Presented) The method according to claim 29, wherein said lymphoid cell is a chicken Bursal lymphoma cell.

49. (Previously Presented) The method according to claim 29, wherein said lymphoid cell is a DT40 cell or a derivative thereof.

50. (Previously Presented) The method according to claim 29, wherein said target nucleic acid sequence encodes a protein or expresses a regulatory activity.

51. (Previously Presented) The method according to claim 29, wherein said target nucleic acid encodes a protein selected from the group consisting of an immunoglobulin chain, a selection marker, a DNA-binding protein, a DNA-binding protein fragment, an enzyme, a receptor protein, and a receptor protein fragment.

52. (Previously Presented) The method according to claim 29, wherein said target nucleic acid sequence is a human immunoglobulin V-gene or a part thereof.

53. (Previously Presented) The method according to claim 29, wherein said target nucleic acid sequence comprises a transcription regulatory element or an interfering RNA (RNAi) sequence.

54. (Previously Presented) The method according to claim 53, wherein said transcription regulatory element is a promoter.

55. (Previously Presented) The method according to claim 29, further comprising identifying said genetically modified lymphoid cell containing said target nucleic acid sequence.

56. (Previously Presented) The method according to claim 55, wherein said identifying said genetically modified lymphoid cell containing said target nucleic acid sequence

comprises identifying a protein encoded by said target nucleic acid sequence on the surface of said genetically modified lymphoid cell, within said genetically modified lymphoid cell, or outside of said genetically modified lymphoid cell.

57. (Withdrawn) The method according claim 30, further comprising modulating said selective genetic diversification of said transgenic target nucleic acid sequence by varying the number, the orientation, the length or the degree of homology of said nucleic acid sequence capable of serving as a gene conversion donor.

58. (Currently Amended) The method according to claim 29, further comprising modulating said selective genetic diversification of said transgenic target nucleic acid sequence with a DNA repair or recombination factor other than a XRCC2, XRCC3, or RAD51 protein or their analogues.

59. (Previously Presented) The method according to claim 58, wherein said DNA repair or recombination factor is a RAD54 protein.

60. (Currently Amended) A method for producing a genetically modified lymphoid cell capable of directed and selective genetic diversification of a transgenic targeted nucleic acid sequence by hypermutation comprising transfecting a lymphoid cell with a genetic construct containing said transgenic target nucleic acid sequence, wherein said transgenic target nucleic acid sequence is inserted into a chromosome of said lymphoid cell and said genetic construct further comprises a nucleic acid sequence capable of directing genetic diversification, said lymphoid cell is capable of gene conversion prior to transfection, and said hypermutation in said genetically modified lymphoid cell occurs at a rate higher than the background mutation rate of mutation in said lymphoid cell.

61. (Previously Presented) The method according to claim 60, wherein said genetic construct is inserted into said chromosome of said lymphoid cell at a particular location by targeted integration.

62. (Withdrawn) The method according to claim 61, wherein said genetic construct is inserted into a chromosome of said lymphoid cell at a random chromosomal position.

63. (Previously Presented) The method according to claim 29, wherein said lymphoid cell comprises a functional AID protein and has no pseudo-V genes.

64. (Previously Presented) The method according to claim 60, wherein said lymphoid cell comprises a functional AID protein and has no pseudo-V genes.

65. (Previously Presented) The method according to claim 29, wherein said hypermutation is at a rate above an order of 10^{-9} to 10^{-10} bp⁻¹ generation⁻¹.

66. (Previously Presented) The method according to claim 60, wherein said hypermutation is at a rate above an order of 10^{-9} to 10^{-10} bp⁻¹ generation⁻¹.

67. (Previously Presented) The method according to claim 29, wherein said hypermutation is at a rate between 10^{-5} to 10^{-3} bp⁻¹ generation⁻¹.

68. (Previously Presented) The method according to claim 60, wherein said hypermutation is at a rate between 10^{-5} to 10^{-3} bp⁻¹ generation⁻¹.

69. (Previously Presented) The method according to claim 29, wherein the rate of hypermutation in said genetically modified lymphoid cell is at least ten times higher than the mutation rate in said lymphoid cell.

70. (Previously Presented) The method according to claim 60, wherein the rate of hypermutation in said genetically modified lymphoid cell is at least ten times higher than the mutation rate in said lymphoid cell.

71. (Previously Presented) The method of claim 29, wherein said lymphoid cell is derived from animal species which use the mechanism of gene conversion as a primary mechanism for developing their immunoglobulin repertoire.

72. (New) The method of claim 29, wherein said transgenic target nucleic acid sequence is in the absence of an adjacent donor sequence capable of serving as a gene conversion donor for said transgenic target nucleic acid sequence.

73. (New) The method of claim 60, wherein said transgenic target nucleic acid sequence is in the absence of an adjacent donor sequence capable of serving as a gene conversion donor for said transgenic target nucleic acid sequence.